

**UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF GEORGIA  
ATLANTA DIVISION**

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MIMEDX GROUP, INC.,

Plaintiff,

v.

U.S. FOOD AND DRUG  
ADMINISTRATION; U.S.  
DEPARTMENT OF HEALTH AND  
HUMAN SERVICES; XAVIER  
BECERRA, in his official capacity as  
Secretary of Health and Human  
Services; and ROBERT M. CALIFF,  
M.D., in his official capacity as  
Commissioner of Food and Drugs,  
U.S. Food and Drug Administration,

Defendants.

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Case No.: \_\_\_\_\_

**COMPLAINT**

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## **NATURE OF THE ACTION**

1. Plaintiff MiMedx Group, Inc. (“MiMedx”) brings this action under the Administrative Procedure Act to hold unlawful and set aside FDA’s final decision classifying MiMedx’s wound-care product AXIOFILL as a biological product subject to regulation by the Center for Biologics Evaluation and Research. FDA’s final decision is attached as Exhibit A.

2. AXIOFILL is a dry particulate consisting of extracellular matrix (or “ECM”) from human placental tissue that is donated by living mothers who have delivered healthy babies. The placental disc ECM comprises an intricate network of large molecules that provide a “scaffold” supporting the ingrowth of new cells. In manufacturing, the cells are removed, leaving the placental disc ECM intact.

3. Under FDA’s regulations, AXIOFILL should be classified not as a biological product, but as a “361 HCT/P.” This term refers to human cells, tissues, and cellular and tissue-based products (“HCT/Ps”) that meet FDA’s criteria to be regulated solely under section 361 of the Public Health Service Act, and not under the distinct statutory authorities that govern drugs, devices, and biological products.

4. As MiMedx demonstrated in its submissions to FDA, AXIOFILL

meets all the regulatory criteria to be classified as a 361 HCT/P. In particular, AXIOFILL is composed solely of human tissue—placental disc ECM—that (i) is “minimally manipulated,” meaning it is processed in ways that preserve its original ability to serve as a scaffold for cellular ingrowth; (ii) is intended for “homologous use,” meaning it performs the same basic function (providing a scaffold for cellular ingrowth) in the recipient as in the donor; (iii) is not combined with any prohibited articles; and (iv) does not have a systemic effect on the body or depend on the metabolic activity of living cells. In fact, more than 20 years ago FDA issued a formal, binding decision in which it classified an essentially identical wound-care product derived from human placental tissue as a 361 HCT/P.

5. Despite all this, FDA concluded that AXIOFILL does not qualify as a 361 HCT/P because it is more than “minimally manipulated.” In reaching that conclusion, FDA contravened the plain text of its own regulations. *See* 21 C.F.R. §§ 1271.3, 1271.10. FDA applied the wrong analysis, asking whether AXIOFILL retained the characteristics of *the original placental disc as a whole*—including its ability to serve as a “selective barrier” between “the fetal and maternal circulatory systems” in the tissue *donor*—instead of determining whether AXIOFILL retains the characteristics of *the placental disc ECM* that are relevant to its ability to serve as a scaffold for cellular ingrowth in the

tissue *recipient*. In a closely related context, the Eleventh Circuit chastised FDA for the same conceptual error of evaluating whether a product qualified as a 361 HCT/P by focusing not on the specific product at issue, but on the larger organ or tissue from which that product was derived.

6. FDA also provided no adequate explanation for departing from its own precedent, including its decision classifying an essentially identical product as a 361 HCT/P. In addition, there is no logical way to reconcile FDA's longstanding position that "demineralized bone matrix" powder is a 361 HCT/P with its conclusion that AXIOFILL is not a 361 HCT/P. Complicating matters further still, while MiMedx's request for classification of AXIOFILL was pending before FDA, the agency classified a substantially similar product as a device rather than a biological product. These zigzagging classification decisions constitute arbitrary and capricious decision-making.

7. MiMedx seeks a declaratory judgment and injunctive relief. The Court should vacate FDA's designation of AXIOFILL as a biological product; declare that FDA's designation of AXIOFILL as a biological product is arbitrary, capricious, an abuse of discretion, and contrary to law; and declare that AXIOFILL meets the criteria to be regulated solely under section 361 of the Public Health Service Act (*i.e.*, that AXIOFILL is a 361 HCT/P).

## **PARTIES**

8. Plaintiff MiMedx Group, Inc. is a corporation organized and existing under the laws of the State of Florida. MiMedx is registered to do business in Georgia and maintains its headquarters and principal place of business at 1775 West Oak Commons Ct. NE, Marietta, Georgia 30062.

9. Defendant FDA, which has its principal office at 10903 New Hampshire Avenue, Silver Spring, Maryland 20993, is a federal agency headquartered in Maryland. It regulates drugs and medical devices under authority delegated by Congress and the Secretary of Health and Human Services.

10. Defendant U.S. Department of Health and Human Services, which has its principal office at 200 Independence Avenue SW, Washington, D.C. 20201, is a federal agency headquartered in the District of Columbia. It has authority over FDA.

11. Defendant Xavier Becerra is being sued in his official capacity as Secretary of Health and Human Services. As Secretary, Mr. Becerra has ultimate responsibility for the activities of the Department of Health and Human Services, including those actions complained of herein. Mr. Becerra maintains an office at 200 Independence Avenue SW, Washington, D.C. 20201.

12. Defendant Robert Califf, M.D., is being sued in his official capacity

as Commissioner of Food and Drugs, FDA. As Commissioner, Dr. Califf has responsibility for the activities of FDA, including those actions complained of herein. Dr. Califf maintains an office at 10903 New Hampshire Avenue, Silver Spring, Maryland 20993.

### **JURISDICTION AND VENUE**

13. This Court has original subject matter jurisdiction over this action pursuant to 28 U.S.C. § 1331 because it arises under the laws of the United States.

14. MiMedx has a right to bring this action pursuant to the Administrative Procedure Act (“APA”), 5 U.S.C. §§ 701–706, and the Declaratory Judgment Act, 28 U.S.C. § 2201.

15. There is an actual, justiciable controversy between the parties concerning whether FDA’s decision to classify AXIOFILL as a biological product rather than a 361 HCT/P is consistent with the requirements of the Federal Food, Drug, and Cosmetic Act (“FDCA”), 21 U.S.C. § 301 *et seq.*, the Public Health Service Act (“PHSA”), 42 U.S.C. § 201 *et seq.*, FDA’s regulations, and the APA.

16. Venue is proper in this District pursuant to 28 U.S.C. § 1391(e) because this is a civil action in which the defendants are officers or agencies of the United States, MiMedx resides in this District, and no real property is

involved in this action.

## **STATUTORY AND REGULATORY BACKGROUND**

17. The FDCA grants FDA the authority to regulate certain categories of medical products, including drugs, devices, and biological products.

18. In 2001, FDA established a “comprehensive new system of regulation” for human cells, tissues, and cellular and tissue-based products, or “HCT/Ps.” Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing, 66 Fed. Reg. 5447, 5447–48 (Jan. 19, 2001). FDA’s regulations governing HCT/Ps are codified primarily in Part 1271 of Title 21 of the Code of Federal Regulations. *See* 21 C.F.R. §§ 1271.1–1271.440.

19. FDA defines HCT/Ps as “articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.” 21 C.F.R. § 1271.3(d). Examples of HCT/Ps “include, but are not limited to, bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue.” *Id.*

20. Since 2001, FDA has followed a “tiered, risk-based approach” to regulating HCT/Ps. 66 Fed. Reg. at 5448. Under this approach, “most HCT/Ps”

are “regulated solely under” section 361 of the Public Health Service Act, which authorizes FDA to make and enforce regulations to prevent the spread of infectious disease. *Id.* at 5449–51; *see* 42 U.S.C. § 264(a). HCT/Ps that meet FDA’s criteria to be regulated solely under section 361 are called “361 HCT/Ps.” 66 Fed. Reg. at 5449. HCT/Ps that do *not* meet those criteria are classified by FDA as drugs, devices, and/or biological products, all of which are subject to different regulation, including premarket review. *Id.*

21. To qualify as a 361 HCT/P, an HCT/P must meet four regulatory criteria set out in 21 C.F.R. § 1271.10(a):

a. *First*, the HCT/P must be “minimally manipulated.” *Id.* § 1271.10(a)(1). “For structural tissue,” FDA defines minimal manipulation as “processing that does not alter the original relevant characteristics of the tissue relating to the tissue’s utility for reconstruction, repair, or replacement.” *Id.* § 1271.3(f)(1).

b. *Second*, the HCT/P must be “intended for homologous use only.” *Id.* § 1271.10(a)(2). FDA defines homologous use as “repair, reconstruction, replacement, or supplementation of a recipient’s cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor.” *Id.* § 1271.3(c).

c. *Third*, the HCT/P’s manufacture must not “involve the

combination of cells or tissues with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent, provided that the addition of water, crystalloids, or the sterilizing, preserving, or storage agent does not raise new clinical safety concerns with respect to the HCT/P.” *Id.* § 1271.10(a)(3).

d. *Fourth*, the HCT/P must either (i) not have a “systemic effect” and not be “dependent upon the metabolic activity of living cells for its primary function,” or (ii) comply with use limitations that are not relevant here. *Id.* § 1271.10(a)(4).

22. An establishment that manufactures a 361 HCT/P must register with FDA and submit to FDA a list of each HCT/P it manufactures. *Id.* §§ 1271.1(b)(1), 1271.10(b), 1271.21–.37. It also must comply with FDA’s “current good tissue practice” (or “CGTP”) regulatory requirements, which govern, among other things, the screening and testing of cell and tissue donors and the recovery, processing, storage, labeling, packaging, and distribution of HCT/Ps. *Id.* § 1271.145; *see id.* §§ 1271.45–.320. And it must also comply with additional requirements that are specific to 361 HCT/Ps, including requirements related to reporting, labeling, inspection, and enforcement. *Id.* §§ 1271.330–.440.

23. If an HCT/P does not meet the criteria to be classified as a 361

HCT/P (and does not qualify for any of the regulatory exceptions in § 1271.15), FDA may regulate the HCT/P as a drug or device under the Federal Food, Drug, and Cosmetic Act or as a biological product under the Public Health Service Act. *Id.* § 1271.20. Drugs, devices, and biological products are all subject to different regulation than 361 HCT/Ps. *See, e.g.*, 21 U.S.C. § 355 (drugs); *id.* § 360c (devices); 42 U.S.C. § 262 (biological products). For example, and as relevant here, it is generally unlawful to distribute a biological product in interstate commerce without first obtaining premarket approval from FDA by submitting a “biologics license application.” *See* 42 U.S.C. § 262(a).

24. A product sponsor may submit a request for designation, or “RFD,” to obtain a formal, binding determination from FDA as to the product’s classification. 21 U.S.C. § 360bbb-2(a); 21 C.F.R. § 3.7. FDA must respond to the RFD within 60 days; if it fails to do so, the sponsor’s recommended classification becomes final. 21 U.S.C. § 360bbb-2(b)–(c); 21 C.F.R. § 3.8(b). A classification made through the RFD process cannot be changed “except with the written consent of the [sponsor], or for public health reasons based on scientific evidence.” 21 U.S.C. § 360bbb-2(b)–(c); 21 C.F.R. § 3.9.

25. FDA’s decision on an RFD constitutes final agency action that is reviewable under the APA. *See, e.g., Genus Med. Techs. LLC v. FDA*, 994 F.3d 631, 636 (D.C. Cir. 2021).

26. FDA also invites product sponsors to obtain “informal, non-binding feedback” regarding a product’s classification by submitting a Pre-Request for Designation, or “Pre-RFD.” FDA, How to Prepare a Pre-Request for Designation (Pre-RFD): Guidance for Industry at 3 (Feb. 2018). FDA’s “goal is to provide feedback on a pre-RFD within 60 calendar days.” *Id.* at 7.

## GENERAL ALLEGATIONS

### A. MiMedx’s AXIOFILL Product

27. MiMedx is a pioneering biomedical company based in Marietta, Georgia. With more than a decade of experience helping clinicians manage chronic and other hard-to-heal wounds, MiMedx provides a leading portfolio of products for wound-care, burn, and surgical applications.

28. One such wound-care product is AXIOFILL, which MiMedx launched in September 2022. In technical terms, AXIOFILL is a decellularized particulate human placental connective tissue matrix that is intended to replace or supplement damaged or inadequate integumental tissue. It can be applied to wounds—including large, complex, or irregularly shaped wounds—to provide a scaffold for cellular ingrowth.

29. Human tissue contains both living cells and extracellular matrix (or “ECM”). ECM is an intricate network of macromolecules that provides structural support for the surrounding cells. AXIOFILL consists of ECM that

is sourced from donated human placental disc tissue, which is collected from living mothers immediately following the delivery of healthy babies. The tissue is processed through a series of soak and rinse steps that remove cellular components and wash away the cellular components and other non-intrinsic material, such as maternal blood, debris from maternal and/or fetal tissues, and microorganisms. These steps leave the ECM intact. Therefore, only placental disc ECM remains in the final product, which is cut and ground into particles approximately 1 millimeter in diameter, as shown in Figure 1. The resulting particulate is applied to wounds as shown in Figure 2, either in a dry state or hydrated with sterile saline to form a paste, and acts as a scaffold to support the ingrowth of new cells.

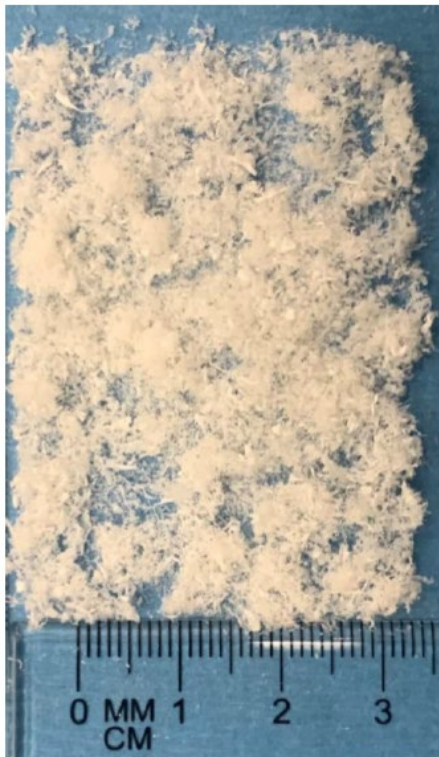


Figure 1 – Photo of AXIOFILL



Figure 2 – Use of AXIOFILL

30. Before marketing, MiMedx determined that AXIOFILL met all the regulatory criteria to qualify as a 361 HCT/P because it is composed solely of placental disc ECM that is minimally manipulated, is intended for homologous use, is not combined with prohibited articles, and does not have a systemic effect or depend on the metabolic activity of living cells.

31. MiMedx therefore complied with all applicable regulatory requirements in 21 C.F.R. Part 1271, and it did not seek premarket approval for AXIOFILL under the statutory provisions applicable to drugs and biological

products. *See Richfield v. PolarityTE, Inc.*, 2023 WL 3010208, at \*2 (D. Utah Apr. 19, 2023) (“[T]he regulations allow companies, in the first instance, to determine whether a product meets the Section 361 registration requirements (including, for example, whether the HCT/P is minimally manipulated). There is no provision in the PHSA or the implementing regulations that requires consultation with or approval by the FDA prior to Section 361 registration of a product.” (citation omitted)).

**B. FDA’s Inspection of MiMedx’s Facilities, Pre-RFD Assessment of AXIOFILL, and Warning Letter**

32. In February and March 2023, FDA inspected MiMedx’s facilities in Marietta and Kennesaw, Georgia. At the conclusion of the inspection, FDA investigators issued a “Form 483” for each facility purporting to describe significant regulatory deviations applicable to AXIOFILL based on the position that AXIOFILL is a biological product, not a 361 HCT/P. *See* Ex. B; Ex. C. These forms stated that they contained “inspectional observations” that did “not represent a final Agency determination regarding your compliance.” Ex. B at 1; Ex. C at 1. The FDA investigators encouraged MiMedx to seek an official classification determination for AXIOFILL.

33. On March 22, 2023, MiMedx submitted a Pre-Request for Designation (“Pre-RFD”) requesting an informal, preliminary assessment and

determination that AXIOFILL was properly classified as a 361 HCT/P. *See* Ex. D.

34. Also on March 23, 2023, MiMedx submitted written responses to FDA's Form 483s. *See* Ex. E; Ex. F. MiMedx explained that it believed AXIOFILL met all the requirements for regulation as a 361 HCT/P and that it had submitted a Pre-RFD to that effect. MiMedx also pointed out that AXIOFILL did not present any known safety concerns, as MiMedx had distributed more than 3,000 units of AXIOFILL and had not received a single complaint related to product safety or adverse experiences.

35. On March 31, 2023, FDA issued questions regarding the Pre-RFD, to which MiMedx responded on April 24, 2023. *See* Ex. G.

36. On May 3, 2023, FDA issued additional questions, to which MiMedx responded on May 12, 2023. *See* Ex. H.

37. FDA responded to the Pre-RFD on October 18, 2023, nearly seven months after MiMedx's submission. *See* Ex. I.

38. FDA's Pre-RFD response letter stated that the agency's "preliminary assessment is that your product appears to be an HCT/P that does not meet all the criteria set forth in 21 CFR 1271.10(a) for regulation solely under section 361." Ex. I at 2. Specifically, FDA stated that AXIOFILL did not appear to qualify as "minimally manipulated" because the donated placental

tissue was processed in ways that altered its “original relevant characteristics” relating to its “utility to act as a selective barrier that provides a transport function between different circulatory systems (e.g., the fetal and maternal circulatory systems).” *Id.* at 3–4. In a footnote, FDA stated without further explanation that AXIOFILL “also does not appear to meet other criteria in 1271.10(a), including, for example, 1271.10(a)(2).” *Id.* at 6 n.16. FDA concluded that AXIOFILL “appears to be a biological product.” *Id.* at 6.

39. FDA’s Pre-RFD response letter stated that “this response does not constitute final agency action and if you would like a final determination with respect to the classification or jurisdictional assignment of your product, you would need to submit an RFD in accordance with 21 CFR 3.7.” *Id.* 8.

40. On October 23, 2023, MiMedx updated its responses to FDA’s Form 483s, informing FDA that it would submit a formal Request for Designation for AXIOFILL on or before December 31, 2023. *See* Ex. J; Ex. K.

41. On December 20, 2023, FDA issued MiMedx a warning letter. *See* Ex. L.

42. In its warning letter, FDA acknowledged that AXIOFILL is an HCT/P but asserted that AXIOFILL “fails to meet the minimal manipulation criterion” to be regulated as a 361 HCT/P. *Id.* at 1–2. Instead, FDA stated that AXIOFILL is subject to regulation as both a drug and a biological product. FDA

therefore claimed that MiMedx had broken the law by marketing AXIOFILL without first obtaining a biologics license from FDA, as well as by failing to comply with various regulatory requirements applicable to biological products but not to 361 HCT/Ps.

**C. MiMedx's Formal Request for Designation of AXIOFILL**

43. On December 22, 2023, MiMedx submitted an RFD requesting that FDA formally designate AXIOFILL as a 361 HCT/P. FDA responded on January 2, 2024, stating that the RFD was not filed because it did not contain all the information required by FDA's regulations.

44. MiMedx amended and resubmitted the RFD on January 12, 2024. *See Ex. M.*

45. FDA accepted the amended RFD for review and deemed it filed on January 22, 2024. *See Ex. N.*

46. In the RFD, MiMedx demonstrated that AXIOFILL satisfies each of the criteria in 21 C.F.R. § 1271.10(a) for classification as a 361 HCT/P. MiMedx also responded in detail to FDA's preliminary assessment that AXIOFILL was more than minimally manipulated, explaining that FDA's reasoning was contrary to the text of the regulations and arbitrarily departed from FDA's other classification decisions regarding materially indistinguishable products.

***MiMedx Showed that AXIOFILL Meets All  
the Criteria for Classification as a 361 HCT/P***

47. MiMedx’s RFD demonstrated that AXIOFILL satisfies each of the regulatory criteria for classification as a 361 HCT/P.

48. *First*, MiMedx explained that AXIOFILL is minimally manipulated under 21 C.F.R. § 1271.10(a)(1) because the manufacturing process “does not alter the original relevant characteristics” of the placental disc ECM relating to its “utility for reconstruction, repair, or replacement,” namely, its “capacity to allow cellular ingrowth.” Ex. M at 8 (quoting § 1271.3(f)(1)); *see id.* at 4–5 (summarizing results of mouse study demonstrating ingrowth of cells into AXIOFILL). MiMedx also noted that FDA had long recognized that the processing steps used to make AXIOFILL—including cutting, decellularization, lyophilization, and grinding of structural tissue—are minimal manipulation. *See id.* at 8 n.6.

49. *Second*, MiMedx explained that AXIOFILL is intended for homologous use, 21 C.F.R. §§ 1271.10(a)(2), 1271.3(c), because the placental disc ECM performs the “same basic function (providing a scaffold for cellular ingrowth) in the recipient as in the donor.” Ex. M at 10. MiMedx noted FDA’s prior assurances that it would “interpret nonhomologous narrowly” and that the “use of a structural tissue may be homologous even when it does not occur

in the same location as it occurred in the donor.” *Id.* (quoting 66 Fed. Reg. at 5458).

50. *Third*, MiMedx explained that AXIOFILL satisfies the criterion in 21 C.F.R. § 1271.10(a)(3) because it is “composed solely of placental disc ECM” that “is not combined with another article, except for water, crystalloids, or a sterilizing, preserving, or storage agent,” and “[t]he manufacturing agents are all commonly used in human tissue processing and do not raise new clinical safety concerns.” Ex. M at 11.

51. *Fourth*, MiMedx explained that AXIOFILL satisfies the criterion in 21 C.F.R. § 1271.10(a)(4)(i) because it “does not have a systemic effect” and “does not contain living cells, and therefore is not dependent on living cells for its primary function.” Ex. M at 11.

***MiMedx Showed that FDA’s Preliminary  
Assessment Misapplied the Regulations***

52. MiMedx also showed that FDA’s preliminary assessment that AXIOFILL was more than minimally manipulated was contrary to the plain text of the regulations for at least two independent reasons.

53. *First*, MiMedx explained that FDA’s preliminary assessment focused on the wrong unit of analysis. FDA asked whether AXIOFILL retained the ability to act as a selective barrier between maternal and fetal circulatory

systems, which is a characteristic of the original placenta or placental disc *as a whole*. AXIOFILL, however, comprises only the *placental disc ECM*. Under the operative provision, the correct unit of analysis is “[t]he HCT/P” that is being “regulated,” which is the HCT/P that is “manufacture[d]” and “intended for ... use” in a patient—not any larger tissue or organ from which that regulated HCT/P was derived, processed, or extracted. 21 C.F.R. § 1271.10(a)(1)–(4).

54. FDA therefore should have focused its minimal-manipulation analysis on the characteristics of the placental disc ECM, not the placenta or placental disc as a whole. *See* Ex. M at 9; *cf. United States v. U.S. Stem Cell Clinic, LLC*, 998 F.3d 1302, 1311 (11th Cir. 2021) (where clinic extracted stem cells from adipose tissue for implantation or transfer, the “proper benchmark” for assessing whether the product was a 361 HCT/P under § 1271.10(a) was the stem cells in particular, not the adipose tissue as a whole).

55. *Second*, MiMedx explained that FDA’s preliminary assessment incorrectly assumed that minimal manipulation requires preserving characteristics of the tissue that relate to its utility in the donor as opposed to the recipient.

56. To qualify as minimal manipulation under the regulations, processing of structural tissue need not preserve *all* original characteristics of

the donated tissue, but only those that relate to “the tissue’s utility for reconstruction, repair, or replacement.” 21 C.F.R. § 1271.3(f)(1). The regulation’s language plainly refers to utility in the tissue *recipient* (here, a patient with a skin wound), as the tissue *donor* has no need for “reconstruction, repair, or replacement.” It follows that even if the placental disc tissue as a whole were the proper unit of analysis, the ability of that tissue to act as a selective barrier between maternal and fetal circulatory systems would not be a “relevant” characteristic that minimal manipulation must preserve, because it has no bearing on the tissue’s “utility for reconstruction, repair, or replacement” in the recipient (*i.e.*, replacing or supplementing damaged or inadequate integumental tissue and serving as a scaffold for cellular ingrowth). *See* Ex. M at 9–10.

57. MiMedx also responded to FDA’s unexplained suggestion that AXIOFILL “does not appear to meet” the requirement in § 1271.10(a)(2) that it be “intended for homologous use only.” Ex. I at 2, 6 n.16. MiMedx noted that while FDA provided “no explanation or analysis to support that conclusion,” it appeared likely that FDA was “led astray by the same errors discussed above, *e.g.*, focusing on the placental disc as a whole rather than the placental disc ECM as the unit of regulatory analysis”—an approach that would be contrary to the regulatory text and the Eleventh Circuit’s decision in *U.S. Stem Cell*

*Clinic*. Ex. M at 10–11.

***MiMedx Showed that FDA’s Preliminary Assessment  
Was Inconsistent with the Agency’s Prior Decisions***

58. MiMedx also demonstrated that FDA’s position that AXIOFILL is more than minimally manipulated was inconsistent with FDA’s other decisions and guidance, thus violating the “fundamental principle of administrative law that agencies must treat like cases alike.” Ex. M at 8 (quoting *Grayscale Invs., LLC v. SEC*, 82 F.4th 1239, 1242 (D.C. Cir. 2023)).

59. MiMedx noted that FDA had previously classified an essentially identical product as a 361 HCT/P. *Id.* at 8, 11–14. In 2004, FDA issued a formal decision in RFD 2004.046, which FDA produced to MiMedx in redacted form pursuant to a Freedom of Information Act request. *See* Ex. D at 32–36. The 2004 decision concluded that “[redacted] human placental connective tissue [redacted] intended to replace or supplement damaged or inadequate integumental tissue” met all the criteria for regulation as a 361 HCT/P. *Id.* at 34–36.

60. That same year, the Tissue Reference Group, a unit within FDA that was created “to provide a single reference point” for questions concerning the classification of HCT/Ps, announced publicly that it had concluded that “[d]ecellularized particulate human placental connective tissue matrix

intended to replace or supplement damaged or inadequate integumental tissue is considered a 361 HCT/P.” *Id.* at 23, 29. Accordingly, although the words “decellularized,” “particulate,” and “matrix” do not appear in the redacted version of FDA’s 2004 RFD response, MiMedx reasonably inferred that those terms appear in the redacted language. MiMedx further explained that AXIOFILL is “essentially the same as the product described in RFD 2004.046.” Ex. M at 12.

61. In its Pre-RFD preliminary assessment, FDA purported to distinguish AXIOFILL from the product described in RFD 2004.046 on the ground that the latter was derived from a portion of the placental disc called the “chorionic plate,” whereas AXIOFILL is derived from the entire placental disc, *including* the chorionic plate. *See* Ex. I at 5. MiMedx explained that this purported distinction is irrelevant because the placental disc is “an interconnected matrix with inseparable zones grossly identified by approximation to the maternal or fetal interface,” and “[r]egardless of zone,” “the function of the ECM will be the same”—to “provide[ ] essential physical scaffolding for the cellular constituents.” Ex. M at 12.

62. MiMedx also presented scientific evidence rebutting FDA’s purported distinction. MiMedx noted that a marketed product called “Interfyll,” manufactured by Celularity, Inc., was a decellularized particulate placental

connective tissue matrix with the same intended use as AXIOFILL. *Id.* at 12–13. Based on Celularity’s public statements, MiMedx inferred that Interfyl was the subject of RFD 2004.046. *See id.* at 13 n.10; *see also* Ex. D at 39. MiMedx presented a study comparing the ingrowth of cells into AXIOFILL versus Interfyl in a nude mouse, which demonstrated that AXIOFILL and Interfyl both retained the relevant characteristics to serve as a scaffold for cellular ingrowth. *See* Ex. M at 12–14.

63. In addition, MiMedx pointed out that FDA’s preliminary assessment of AXIOFILL was inconsistent with FDA’s longstanding position that demineralized bone matrix (“DBM”) powder is minimally manipulated. *Id.* at 15; *see, e.g.*, FDA, Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. 26,744, 26,749 (May 14, 1998) (concluding that “demineralized bone products ... fall[ ] within the minimal manipulation definition”); FDA, Jurisdictional Update: Human Demineralized Bone Matrix (Feb. 16, 2018) (Ex. O) (“Demineralized bone matrix alone (i.e., not combined with any other component) meets the criteria listed above for regulation solely under section 361.”).

64. Just as AXIOFILL is used as a scaffold to support cellular ingrowth in integumental tissue, DBM powder is used as a scaffold to support

cellular ingrowth in bone. Of course, DBM powder does not retain all the characteristics of the original bone *as a whole*—for example, as a demineralized powder, it lacks the ability to support the body and protect internal structures with strength and resistance to compression. Yet FDA has correctly concluded that DBM powder is minimally manipulated because it retains the characteristics that are relevant to its ability to serve as a scaffold for cellular ingrowth in the recipient. Applying that same mode of analysis to AXIOFILL leads to the conclusion that AXIOFILL, too, is minimally manipulated. *See* Ex. M at 15.

#### **D. FDA’s Final Decision on the Request for Designation**

65. On March 22, 2024, FDA issued its final decision in response to MiMedx’s RFD, concluding that AXIOFILL is a biological product and not a 361 HCT/P. *See* Ex. A at 1, 3.

66. FDA determined that AXIOFILL is not “minimally manipulated” as required by 21 C.F.R. § 1271.10(a). In reaching that conclusion, FDA doubled down on its position that in order to be considered minimally manipulated, AXIOFILL would have to retain the original characteristics of “the placental disc as a whole” that relate to “how [the placental disc] functions in the donor,” rather than the original characteristics of the placental disc ECM that relate to its utility for reconstruction, repair, or replacement in the

recipient. Ex. A at 4–6.

67. FDA thus concluded that AXIOFILL is not minimally manipulated because it is processed in a way that alters “the native placental disc’s cohesive physical three-dimensional structure,” thereby affecting the placental disc’s “utility to act as a selective barrier that provides a transport function between ... the fetal and maternal circulatory systems.” *Id.* at 4, 7–8. FDA disregarded (and did not dispute) MiMedx’s evidence that AXIOFILL retains the characteristics of the placental disc ECM that allow it to serve as a scaffold for cellular ingrowth, *see* Ex. M at 12–14, reasoning that “acting as a scaffold for the infiltration of cells” is not a “relevant characteristic of the placental disc” as a whole, Ex. A at 10.

68. In a footnote, FDA dismissed the Eleventh Circuit’s decision in *U.S. Stem Cell Clinic* by stating that it involved the homologous-use criterion rather than the minimal-manipulation criterion. *Id.* at 6 n.15. FDA did not explain, however, why it would make sense to interpret “[t]he HCT/P” in § 1271.10(a)(2) to mean the specific tissue comprising the relevant product (*i.e.*, stem cells rather than adipose tissue), while interpreting the same words in § 1271.10(a)(1) to mean the native organ from which that tissue was derived (*i.e.*, the placental disc as a whole rather than the placental disc ECM).

69. FDA also did not explain how its conclusion that AXIOFILL is

more than minimally manipulated can be squared with its conclusion that the product in RFD 2004.046 is minimally manipulated. FDA reiterated that the product in RFD 2004.046 consists of ECM derived from a *portion* of the placental disc (the chorionic plate), whereas AXIOFILL consists of ECM derived from the *entire* placental disc (including the chorionic plate). Ex. A at 8–9. But FDA did not explain why that difference matters or how the product in RFD 2004.046 could have been classified as minimally manipulated under the approach FDA used when evaluating AXIOFILL.

70. Nor did FDA explain how its conclusion that AXIOFILL is more than minimally manipulated can be squared with its conclusion that demineralized bone matrix powder is minimally manipulated. FDA stated that its “DBM Guidance is based on factors that are specific to DBM products,” but it did not explain what those factors are. *Id.* at 11. FDA also stated that “the original relevant characteristics of bone, in contrast to the placental disc ... relate to its utility to support the body and protect internal structures,” but it did not explain how those characteristics of solid bone as a whole are preserved when that bone is processed into a demineralized powder. *Id.*

71. While FDA’s decision focused on the minimal-manipulation criterion, FDA asserted in a footnote that AXIOFILL “also does not appear to meet” the homologous-use criterion. *Id.* at 11 n.27. FDA stated that MiMedx

had not “provided any additional data or information” to show “that acting as a scaffold for skin repair is a basic function of the ECM component of the placental disc as it exists in the donor.” *Id.* But FDA did not dispute (and it is well understood) that ECM’s basic function, in the donor as well as in the recipient, is to provide a scaffold for cellular ingrowth. *See, e.g.*, Ex. M at 10, 12. FDA then stated that because AXIOFILL was more than minimally manipulated, it was “not necessary to address” homologous use or the other criteria in § 1271.10(a). Ex. A at 11 n.27.

72. Having refused to classify AXIOFILL as a 361 HCT/P, FDA concluded that “AXIOFILL is a biological product because it is comprised of placental ECM proteins ... and other proteins ... which are intended to treat injured skin by replacing or supplementing missing or damaged ECM.” *Id.* at 12. FDA further concluded that AXIOFILL is not a device because it “retains components”—such as GAG chains, fibronectin, and laminin—that may support skin healing through “chemical action.” *Id.* at 12–14. FDA did not address past decisions where it has classified products with similar components as devices rather than biologics. *See, e.g.*, Ex. P (wound dressing containing collagen-GAG matrix that “provides a scaffold for cellular invasion”).

### **E. FDA’s Classification of a Similar Product as a Device**

73. Compounding the confusion around FDA’s approach, while MiMedx’s RFD for AXIOFILL was pending before the agency, FDA granted another company clearance to market a substantially similar product as a medical device rather than a biological product.

74. “Corplex P” is a product developed by StimLabs LLC, which describes it as “a human umbilical cord particulate ... for use in the management of [various types of] wounds.” StimLabs LLC, *Corplex P*, <https://stimlabs.com/corplexp/> (accessed Mar. 22, 2024) (Ex. Q). StimLabs states that Corplex P is “derived from human umbilical cord extracellular matrix (ECM)” and “ret[ains] ECM components such as collagen and glycosaminoglycans,” making it valuable “for the management of acute and chronic wounds.” Press Release, StimLabs LLC, FDA Clears Groundbreaking Corplex P™: The First Human Umbilical Cord-Derived Medical Device (Feb. 6, 2024), <https://www.prnewswire.com/news-releases/fda-clears-groundbreaking-corplex-p-the-first-human-umbilical-cord-derived-medical-device-302053994.html> (Ex. R).

75. Corplex P purports to work in much the same way as AXIOFILL. *See, e.g.,* Jenna Philpott, *FDA green lights StimLabs umbilical cord-derived wound graft*, MEDICAL DEVICE NETWORK (Feb. 8, 2024), <https://www.medicaldevice-network.com/news/fda-green-lights-stimlabs-umbilical-cord->

derived-wound-graft/ (Ex. S) (“[Corplex P] claims to be the first graft derived from the human umbilical cord extracellular matrix (ECM), to treat and manage acute and chronic wounds. ... An ECM wound care device works by providing a natural scaffold or structure that mimics the natural environment of cells in the body. Corplex P is made up of components such as collagen and glycosaminoglycans that support cell growth and tissue regeneration.”). An image of Corplex P on StimLabs’ website (Ex. Q) confirms that it has undergone processing similar to AXIOFILL:



Figure 3 – Corplex P

76. On February 2, 2024, FDA cleared Corplex P through the Section 510(k) premarket notification process, which is reserved for medical devices. *See* Ex. T; *see also* 21 U.S.C. § 360(k) (establishing premarket notification process for “device[s] intended for human use”). FDA’s summary letter describes Corplex P as a “particulate device” that is “derived from human

umbilical cord extracellular matrix (ECM) and is indicated for the management of a range of acute and chronic wounds” and is “lyophilized and packaged in a sterile vial, allowing the device to be rehydrated and applied directly to the wound.” Ex. T at 4. FDA did not treat Corplex P as a biological product or require StimLabs to obtain a biologics license before marketing Corplex P.

77. Nothing in FDA’s RFD decision explains why the agency classified AXIOFILL as a biological product and Corplex P as a device.

**CLAIM FOR RELIEF**  
**Violation of the Administrative Procedure Act**  
**5 U.S.C. § 706(2)**

78. MiMedx realleges and incorporates by reference each of the preceding paragraphs as if set forth fully herein.

79. AXIOFILL meets all the regulatory criteria to be regulated solely under section 361 of the Public Health Service Act because it is composed solely of placental disc ECM that is minimally manipulated, is intended for homologous use, is not combined with prohibited articles, and does not have a systemic effect or depend on the metabolic activity of living cells for its primary function.

80. FDA’s final decision violates the APA because it is not in accordance with law, as it conflicts with the applicable statutory and

regulatory requirements. FDA's final decision also violates the APA because it is arbitrary and capricious and an abuse of discretion and does not comply with the requirements of reasoned decision-making.

81. As set forth above, FDA focused on the wrong unit of analysis and contravened Eleventh Circuit precedent by asking whether AXIOFILL retained the relevant characteristics of the placenta or placental disc *as a whole*, rather than the relevant characteristics of the *placental disc ECM*.

82. As set forth above, FDA compounded its error by focusing on characteristics that relate to how the placental disc functions *in the donor*, rather than characteristics that relate to the placental disc ECM's utility for reconstruction, repair, or replacement *in the recipient*.

83. As set forth above, FDA also arbitrarily departed from its own precedent and failed to provide a reasoned explanation for its decision or to respond adequately to reasonable objections.

84. For the reasons set forth above, FDA's final decision lacks an adequate explanation and contradicts the plain text of the applicable regulations, Eleventh Circuit precedent, and FDA's own decisions and actions with regard to substantially similar products, all in violation of the Administrative Procedure Act.

### **PRAYER FOR RELIEF**

MiMedx requests that the Court grant the following relief:

- A. Injunctive relief and a declaratory judgment that:
  - i. Vacates FDA's designation of AXIOFILL as a biological product;
  - ii. Declares that FDA's designation of AXIOFILL as a biological product is arbitrary, capricious, an abuse of discretion, and contrary to law; and
  - iii. Declares that AXIOFILL meets the criteria to be regulated solely under section 361 of the Public Health Service Act (*i.e.*, AXIOFILL is a 361 HCT/P).
- B. An award of costs and attorneys' fees.
- C. Such other and further relief as may be just and proper.

Dated: March 25, 2024

Respectfully submitted,

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